EXHIBIT 3

70901-07600

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Harris and Dunnett
Serial No:	13/356,182
Filed:	January 23, 2012
For:	METHODS AND COMPOSITIONS FOR INCREASING THE ANAEROBIC WORKING CAPACITY IN TISSUES
Examiner:	Raymond J. Henley III
Art Unit:	1629
Conf. No.:	5840

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

PRE-ISSUANCE SUBMISSION PURSUANT TO 37 C.F.R. 1.291

Introduction

This Pre-Issuance Submission Pursuant to 37 C.F.R. 1.291 is being submitted on behalf of Woodbolt Distribution, LLC ("Woodbolt").

Compliance With 37 C.F.R. 1.291

In accordance 37 C.F.R. 1.291, the following requirements have been met:

1. Identification of Application: In accordance with 37 C.F.R. 1.291(a), the pending patent application has been identified above by serial number and filing date.

2. Service on Applicants: In accordance with 37 C.F.R. 1.291(b) and 1.248, this submission is being simultaneously served upon the applicants. A certificate of service is being submitted herewith.

3. Timely Filing: In accordance with 37 C.F.R. 1.291(b), this submission is being submitted before the date the application was published, and, before the date of a Notice of Allowance. Also, in accordance with 37 C.F.R. 1.291(b)(2), this is the first submission in this application by the real party in interest, Woodbolt.

4. Submission of Required Items: In accordance with 37 C.F.R. 1.291(c), the following items are being submitted:

(a) a listing of the patents, publications and other information relied upon in PTO/SB/08a form enclosed herewith;

(b) a concise explanation of the relevance of each item listed in the PTO/SB/08a form is set forth below;

(c) a copy of each listed patent, publication or other item of information in written form, is attached; and

(d) an English translation of all of the necessary and pertinent parts of any non-English language patent, publication or other item of information relied upon.

U.S. Patent No. 5,965,596 is Prior Art To The Present Application

U.S. Patent No. 5,965,596 (" '596 Patent") issued October 12, 1999 is prior art under 35 U.S.C. § 102 (b) to the present application, and this has been confirmed by a ruling from the Office in a related reexamination proceeding.

The present application claims priority to U.S. Serial No. 12/806,356 filed August 30, 2010, which issued as U.S. Patent No. 8,129,422 ("'422 Patent"). The '422 Patent is the subject of an Inter Partes Reexamination (Control No. 95/002,048) filed by Woodbolt. In that reexamination, an Office Action issued on October 16, 2012 which ruled that the '422 Patent was entitled to a priority date no earlier than April 10, 2003 and was not entitled to claim priority

back to the '596 Patent.[1] The Office Action rejected all the claims for which reexamination had been requested relying, *inter alia*, upon the '596 Patent as prior art. A complete explanation of the basis for the rejection is found in that Office Action, a copy of which is being attached, and which is being incorporated by reference herein.

Although applicants cited this Office Action as item 21 in their Information Disclosure Statement filed February 4, 2013, applicants did not explain the relevance of the '422 Patent reexamination to this application, or, point out that the Office had already ruled that the '422 Patent was not entitled to priority back to the '596 Patent, thus making the '596 Patent prior art to the '422 Patent. Because the present application claims priority through the application for the '422 Patent and can have no better claim for priority than that application, the present application is also not entitled to claim the priority of the '596 Patent, thus making the '596 Patent prior art to the present application.

In addition to the '596 Patent, U.S. Patent No. 6,172,098 issued January 9, 2001 on an identical specification, is also prior art under 35 U.S.C. § 102 (b).

Prior Art Cited

1. U.S. Patent No. 5,965, 596

The relevance of the '596 Patent to claim 1 pending in this application is shown in the following claim chart.

[1] The Office Action, first issued on August 17, 2012, was modified on October 16, 2012.

Pending Claim 1	'596 Patent Disclosure
1. A method of increasing anaerobic working capacity in a human subject, the method comprising:	The '596 Patent states: "The methods and compositions can be used to increase beta-alanylhistidine dipeptide by, for example, [in] sportsmen, athletes, body-builders, synchronized swimmers, soldiers, elderly people, horses in competition, working and racing dogs, and game birds, to avoid or delay the onset of muscular fatigue." (3: 50 - 57).
a) providing to the human subject an amount of an amino acid to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in the tissue,	The '596 Patent further states: "In one aspect, the invention features methods and compositions for increasing the anaerobic working capacity of muscle and other tissues" (2: 17 - 19). "The compositions of the invention can induce the synthesis and accumulation of beta-alanylhistidine dipeptides in a human or animal body when introduced into the body" (2:26 - 29).
wherein said amino acid is at least one of: i) beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; ii) an ester of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; or iii) an amide of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; and	The '596 Patent teaches that the said compositions can comprise beta-alanine and esters of beta-alanine (2: 31 - 41). The amino acid, beta-alanine, and its esters and amides are, by definition, not part of a dipeptide, dipeptide or oligopeptide.
b) exposing the tissue to the blood or blood plasma, whereby the concentration of beta-alanylhistidine is increased in the tissue,	The '596 Patent states: "The method includes the steps of providing an amount of beta-alanine to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in a tissue, and exposing the tissue to the blood to blood plasma, whereby the concentration of beta-alanylhistidine is increased in the tissue." (2: 43 - 49).
wherein the amino acid is provided through a dietary supplement.	The '596 Patent discloses providing the compositions of beta-alanine in a dietary supplement for humans (3: 32, 52 - 57; 5: 46 - 49).

The subject matter of claims 2, 4 and 5 (L-histidine) is disclosed in the '596 Patent (2:48-51). Claims 3 and 5 (including creatine) are disclosed in (2:62-67; 5:27-35). Claims 7 and 8 (ingestion, infusion) are disclosed in (9:20-23). Claim 9 is disclosed in (3:9)

2. U.S. Patent No. 6,172,098

This patent contains the same disclosure as the '596 Patent discussed above, and the same explanation of relevancy likewise applies.

Other Prior Art

Applicants' Information Disclosure Statement filed February 4, 2013 merely lists prior art references without any explanation of their relevance, even though applicants were advised of their relevance in the October 16, 2012 Office Action in the '422 Patent reexamination, and that the prior art provided the basis for multiple prior art rejections of the claims in the '422 Patent reexamination.

The claims in the present application are substantially the same as the claims in the '422 Patent whose claims have been rejected in the '422 Patent reexamination. Woodbolt respectfully directs the Examiner's attention to the discussion of these references in the October 16, 2012 Office Action in the '422 Patent reexamination, for their relevancy to the present claims.

Fee

No fee is believed to be due in connection with this Pre-Issuance submission. If any fee is required, please charge Deposit Account No. 02-2275.

Respectfully submitted:

LUCAS & MERCANTI, LLP

Dated: February 8, 2013

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EXAMINER
KUNZ, GARY L

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Transmittal of Communication to Third Party Requester *Inter Partes* Reexamination	Control No. 95/002,048	Patent Under Reexamination 8129422	
	Examiner GARY KUNZ	Art Unit 3991	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

(THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS)

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Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination prceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

THE OFFICE ACTION MAILED 8/17/2012 IS WITHDRAWN. NO RESPONSE IS DUE FROM EITHER PARTY. THE PERIOD FOR RESPONSE TO THIS OFFICE ACTION IS **2 (TW0) MONTHS** FROM THE MAILING DATE OF THIS ACTION FOR PATENT OWNER. THIRD PARTY COMMENTS ON THE PATENT OWNER RESPONSE WILL BE DUE 30 (THIRTY) DAYS FROM THE DATE OF SERVICE OF ANY PATENT OWNER RESPONSE.

Inter Partes Reexamination: Non-Final Action

March 6, 2012: U. S. Patent Application No. 12/806,356, filed August 10, 2010, issued to Harris et al. as U. S. Patent No. 8,129,422.

July 24, 2012: Third Party Requester filed a request for inter partes reexamination of claims 12 – 19 of U. S. Patent No. 8,129,422. This reexamination was assigned control no. 95/002,048.

Priority

Claims 1 - 21 of the '422 patent (patent under reexamination) have an effective filing date of no earlier than April 10, 2003 as explained in detail in the priority discussion in the Order.

The '422 Invention and Claim Interpretation

The '422 patent contains claims 1 - 22. Claims 1 -11 and 20 – 21 are not under reexamination. Claims 12 - 19 are directed to a method of avoiding or delaying the onset of muscle fatigue comprising providing a source of beta-alanine. Independent claim 12 is reproduced below.

Claim 12. A method to avoid or delay the onset of muscular fatigue in a subject comprising:

a) providing to the subject an amount of an amino acid to blood or plasma effective to increase beta-alanylhistidine dipeptide synthesis in muscle tissue, wherein said amino acid is at least one of:

(i) beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide;
(ii) an ester of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; or
(iii) an amide of beta-alanine that is not part of a dipeptide, polypeptide, or oligopeptide; and

b) exposing the muscle tissue to the blood or blood plasma, whereby the concentration of beta-alanylhistidine is increased in the muscle tissue, thereby avoiding or delaying the onset of muscular fatigue,

wherein the amino acid is provided in a dietary supplement, and wherein the subject is not a horse.

The claimed method includes any method of administering beta-alanine to a non-horse subject so that the beta-alanine gets into the blood stream or plasma and then into the muscle tissues. The methods of administration includes ingesting the beta-alanine and infusing it.

The only step of the claimed method that the prior art needs to show to anticipate the claims is the step of ingesting or infusing beta-alanine. All of other "steps" in the claimed method after ingesting or infusing, are inherent in human metabolic and physiological functions. Thus, if beta-alanine is ingested, it will necessarily pass into the gut and from the gut into the blood stream and then into the muscle tissue. As is well-known the muscle tissue will necessarily synthesize the dipeptide, beta-alanylhistidine. The carnosine (beta-alanylhistidine) will necessarily perform the well-known function of buffering hydronium ions and thereby contribute to the delay or avoidance of muscle fatigue in the subject.

Documents Cited by the Requester

This citation of the documents cited by the Requester is repeated to correct numbering and to correlate the naming of the references listed in the request.

1. Harris et al., U. S. Patent No. 5,965,596, issued October 12, 1999 (**Harris '596**).

2. Harris et al., U. S. Patent No. 6,172,098, issued January 19, 2001 (**Harris '098**).

3. Harris et al., U. S. Patent No. 7,504,376, issued March 17, 2009 (**Harris '376**).

4. EP 0 280 593 B1, published June 12, 1991 ("**EP '593**").

5. **Setra**, EP 0 449 787 A2, published June 12, 1991.

6. **Asatoor** et al., "Intestinal absorption of carnosine and its constituent amino acid In man," *Gut*, 11: 250 - 254, 1970.

7. **Gardner** et al., "Intestinal Absorption of the Intact Peptide Carnosine in Man, and Comparison with Intestinal Permeability to Lactulose," *Journal of Physiology* 439: 411 – 422, 1991.

8. **Wu** et al., "Proximate Composition, Free Amino Acids and Peptides Contents in Commercial Chicken and Other Meat Essences," *Journal of Food and Drug Analysis,* 10(3): 170 – 177, 2002.

9. **Li** et al., "Bioactivities of Chicken Essence, *Journal of Food Science*, 17: R105 – R110, 2012. (This document is not prior art because it was published after April 10, 2003 but is only used as evidence).

10. **Bauer** et al., "Biosynthesis of carnosine and related peptides by skeletal muscle cells in primary culture," *Eur. J. Biochem.* 219: 43 - 47, 1994.

11. **Bakardjiev** et al., "Transport of beta-alanine and biosynthesis of carnosine by skeletal muscle cells in primary culture, *Eur. J. Biochem.*, 225: 617 – 623, 1994.

Summary of Grounds of Rejection for 95/002,048

Issue No. in Order	Issue No. in Action	Pages in Request	Claim No.	Prior Art	102 or 103
1	1	13 – 18	12 – 19	Harris '596	102
2	2	20 – 21	12, 13, 17 and 19	Asatoor	102
3	3	21 – 23	12, 17 and 19	EP '593	102
4	4	23 – 24	12, 17 and 19	Gardner	102
5	5	24 – 25	12, 17 and 19	Wu as evidenced by Li	102
6 (No RLP)		26 & 27	12	Setra alone	103
7	7	28-29 & 31-33	12 – 19	Setra in v/o Asatoor	103
8	8	29 & 31-33	12 – 19	Setra in v/o Gardner	103
9	9	29 and 28	12	Setra in v/o Asatoor and Gardner	103
10	10	29 - 33	12 - 19	Setra in v/o Bauer or Bakardjiev	103

Statutory Basis for Claim Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Issue No. 1: Adopted

The Third Party Requester proposes that claims 12 – 19 of the '422 patent are anticipated by Harris '596 as set forth in the request at pages 13 – 18. Issue No. 1 **is adopted** for the following reasons.

Claims 12 – 19 are rejected under 35 USC 102(b) as being anticipated by Harris '596.

The method of claim 12 includes two steps: a) providing to the subject an amount of beta-alanine (or an ester or amide of beta-alanine), as a dietary supplement, to blood plasma . . . and (b) exposing the muscle tissue to the blood or blood plasma. The step of "exposing the muscle tissue to the blood or blood plasma" is inherent in the metabolism or physiology of all subjects, human or animal, to whom the beta-alanine is administered. So the method boils down to providing beta-alanine by 1) ingesting a dietary supplement containing beta-alanine . . . or 2) infusing beta-alanine . . . into the subject's blood.

Claim 12. "A method to avoid or delay the onset of muscle fatigue in a subject . . ."

Harris '596 states, "The methods and compositions can be used to increase beta-alanylhistidine dipeptide by, for example, [in] sportsmen, athletes, body-builders, synchronized swimmers, soldiers, elderly people, horses in competition, working and racing dogs, and game birds, to avoid or delay the onset of muscular fatigue." (3: 50 - 57).

> **. . . comprising: a) providing to the subject an amount of an amino acid to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in muscle tissue. . "**

Harris '596 further states that, "In one aspect, the invention features methods and compositions for increasing the anaerobic working capacity of muscle and other tissues" (2: 17 – 19). The compositions of the invention can induce the synthesis and accumulation of beta-alanylhistidine dipeptides in a human or animal body when introduced into the body" (2:26 - 29).

> **" . . . wherein said amino acid is at least one of:**
> **i) beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide;**
> **ii) an ester of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; or**
> **iii) an amide of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide. . . "**

Harris '596 teaches that the said compositions can comprise beta-alanine and esters of beta-alanine (2: 31 – 41). The amino acid, beta-alanine, and its esters and amides are, by definition, not part of a dipeptide, dipeptide or oligopeptide.

> **" . . . "exposing the muscle tissue to the blood or blood plasma, whereby the concentration of beta-alanylhistidine is increased in the muscle tissue, thereby avoiding or delaying the onset of muscular fatigue . . . "**

Harris '596 states, "The method includes the steps of providing an amount of beta-alanine to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in a tissue, and exposing the tissue to the blood to blood plasma, whereby the concentration of beta-alanylhistidine is increased in the tissue (2: 43 - 49).

> **". . . wherein the amino acid is provided as a dietary supplement wherein the subject is not a horse**."

Harris '596 discloses that the compositions of beta-alanine in a dietary supplement for humans (3: 32, 52 – 57; 5: 46 - 49).

Claim 13 depends from claim 12 and further requires "providing an amount of L-histidine to the blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in the muscle tissue."

Harris '596 teaches that the method can include the step of providing an amount of L-histidine to the blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis (2: 48 - 51).

Claim 14 depends from claim 12 and further requires "increasing the concentration of creatine in the muscle tissue."

Harris '596 discloses that the method can include the step of increasing the concentration of creatine the muscle tissue (2: 62 – 67; 5: 27 - 35).

Claim 15 depends from claim 14 and further requires "providing an amount of L-histidine to the blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in the muscle tissue."

Harris '596 also teaches that the invention can include the ingestion or infusion of beta-alanine and L-histidine, which will necessarily result in the increase of beta-alanylhistidine dipeptide synthesis in muscle tissue (2: 21 – 23; 3: 1 - 4).

Claim 16 depends from claim 12 and further requires "increasing the amount of creatine in the muscle tissue includes providing an amount of creatine to the blood or blood plasma effective to increase the concentration of creatine in the muscle tissue."

Harris '596 discloses that the method of the invention also includes providing creatine to the subjects by ingestion or infusion, thereby increasing the amount of creatine in the blood or blood plasma, which in turn increases the concentration of creatine in tissue such as muscle (2:62 – 67; 5:27 - 35).

Claim 17 depends from claim 12 and further requires that "the providing step is by ingestion."

Harris '596 teaches that the administration of the compositions can be by oral ingestion (2: 21 – 23; 3:28 – 31;).

Claim 18 depends from claim 12 and further requires that "the providing step is by infusion" (2:21 – 23; 3:28 – 31).

Harris '596 teaches that the method of the invention can include oral ingestion or infusion (9: 20 – 23).

Claim 19 depends from claim 12 and further requires that the subject is human.

Harris '596 teaches that the subject can be humans or animals (3:1 - 4: 60 - 67).

In summary, Harris '596 discloses each of the limitations of claims 12 – 19 of the '422 patent. Accordingly, claims 12 – 19 are anticipated by Harris '596.

Issue No. 2: Adopted

The Third Party Requester proposes that claims 12, 13, 17 and 19 of the '422 patent are anticipated by Asatoor as set forth in the request as pages 20 - 21. Issue No. 2 **is adopted** for the following reasons.

Claims 12, 13, 17 and 19 are rejected under 35 USC 102(b) as being anticipated by Asatoor.

Asatoor discloses experiments in which five human test subjects ingested a mixture of beta-alanine and L-histidine (Abstract; pages 250 – 251). Once ingested, the beta-alanine will necessarily be absorbed into the blood stream and from the blood stream into the subject's muscle tissue, the result of which will necessarily increase the beta-alanylhistidine dipeptide synthesis in the muscle tissue. The result will be the avoiding the delay or onset of muscle fatigue. Asatoor thus discloses human subjects ingesting a dietary supplement comprising beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide, which will necessarily be absorbed into the blood stream, and into the muscle tissue to increase beta-alanylhistidine dipeptide synthesis in the muscle tissue to avoid or delay muscle fatigue.

Claim 13 is anticipated because Asatoor teaches that the subjects ingested L-histidine as well as the beta-alanine (Abstract; pages 250 – 251).

Claim 17 is anticipated because Asatoor teaches that the method of administration was by ingestion (Abstract; pages 250 – 251).

Claim 19 is anticipated because Asatoor teaches that the test subjects were human beings (Abstract; pages 250 – 251).

Accordingly, claims 12, 13, 17 and 19 are anticipated by Asatoor.

Issue No. 3: Adopted

The Third Party Requester proposes that claims 12, 17 and 19 of the '422 patent are anticipated by EP '593 as set forth in the request at pages 21 – 23. Issue No. 3 **is adopted** for the following reasons.

Claim 12, 17 and 19 are rejected under 35 USC 102(b) as being anticipated by EP '593.

EP '593 discloses a composition comprising beta-alanine and vitamins for treating cancer [0012]. The beta-alanine can be used individually or in combination with one or more other amino acids such as glycine or taurine [0012]. Finally, the composition can be administered orally (claim 7). EP '593 thus discloses a human dietary supplement comprising beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide as required by claim 12. Once ingested, the beta-alanine will necessarily be absorbed into the blood stream and from the blood stream into the subject's muscle tissue which will necessarily increase beta-alanylhistidine dipeptide synthesis in the muscle to avoid or delay muscular fatigue. The step of ingesting the dietary supplement and the results that necessarily flow from the ingesting anticipate **claim 12** of the '422 patent.

Claim 17 is anticipated because EP '593 teaches that the method of administration was by ingestion (claim 7).

Claim 19 is anticipated because EP '593 teaches the composition is given for the purpose of treating cancer ([0001 - 0032]. The treatment of cancer clearly implies that the subject is a human being,

Issue No. 4: Adopted

The Third Party Requester proposes that claims 12, 17 and 19 of the '422 patent are anticipated by Gardner as set forth in the request at pages 23 – 24. This Issue No. 4 **is adopted** for the following reasons.

Claim 12, 17 and 19 are rejected under 35 USC 102(b) as being anticipated by Gardner.

Gardner discloses an experiment in which a human subject ingested a "test meal" comprising beta-alanine and histidine in syrup.

> "Experimental Procedure"
> Subjects ingested a test meal which was designated (a) 'bland,' (b) 'isotonic' (nominally). . . . All subjects consumed at least one of each test meal . . . . The 'bland' meal comprised 92.5 ml hot water, 7.5 ml Duphulac syrup . . . and 1 g rhamnose (sic) . . . . The Duphulac contained 5 g lactulose and traces of galactose and lactose in aqueous solution. The 'isotonic' test meal contained the same ingredients with the addition of 4 g carnosine . . . . (In an additional experiment on one subject, an approximately isotonic test meal containing 2 g β-alanine plus 2 g histidine instead of carnosine was taken). (pp 412 – 413)

Gardner thus discloses a human subject ingesting a dietary supplement comprising beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide, as required by claim 12. Once ingested, the beta-alanine will necessarily be absorbed into the blood stream and from the blood stream into the subject's muscle tissue, which will necessarily increase the alanylhistidine dipeptide synthesis in the muscle to avoid or delay muscular fatigue.

Thus Gardner anticipates **claim 12** of the Harris '422 patent.

Claim 17 is anticipated because Gardner teaches that the method of administration was by ingestion (Summary 1., pages 412 – 413).

Claim 19 is anticipated because Gardner teaches that the subject was a human being (Summary 1., pages 412 – 413).

Issue No. 5: Adopted

The Third Party Requester proposes that claims 12, 17 and 19 of the '422 patent are anticipated by Wu as evidenced by Li as set forth in the request at pages 24 – 25. Issue No. 5 **is adopted** for the following reasons.

Claims 12, 17 and 19 are rejected under 35 USC 102(b) as being anticipated by Wu as evidenced by Li.

Wu discloses that chicken, beef and fish extracts commonly consumed in Southeast Asia contain beta-alanine.

> In Southwest Asia region, particularly in Chinese communities, chicken essence is consumed as a traditional health food for several ailments, including the use as a nutritional supplement (p. 170).

Table 2 (p. 172) and Table 3 (p. 173) disclose that the essences contain beta-alanine. Table 4 (p. 173) discloses that the essences contain carnosine.

These analyses demonstrate that commercial chicken essences, available in this country as well as Southeast Asia for scores of years, contain a spectrum of amino acids, including beta-alanine as well as carnosine. Wu thus discloses a dietary supplement comprising beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide, which when ingested will necessarily be absorbed into the blood stream,

and into the muscle tissue, which will necessarily increase beta-alanylhistidine dipeptide synthesis in the muscle to avoid or delay fatigue as required by **claim 12.** The step of ingesting the chicken essences taught by Wu anticipates claim 12.

Claim 17 is anticipated because Wu teaches that the essence of chicken containing beta-alanine composition is ingested (page 170).

Claim 19 is anticipated because Wu teaches that the subject is a human being (page 170).

Issue No. 7: Adopted

The Third Party Requester proposes that claims 12 – 19 of the '422 patent are obvious over Setra in view of Asatoor as set forth in the request at pages 28, 29 and 31 – 33. Issue No. 7 **is adopted** for the following reasons.

Claims 12 – 19 are rejected under 35 USC 103(a) as being unpatentable over Setra in view of Asatoor.

Setra discloses pharmaceutical, dietetic or veterinary compositions containing carnosine or peptides related thereto as the active ingredient (page 2, lines 1 - 2). The compositions of Examples 1 and 2 comprise both carnosine and L-histidine (page 2, lines 25 - 37). In particular, Setra discusses the known beneficial properties of these compositions when they are ingested: "Carnosine is a physiological substance, which is present in muscles and in some nervous tissues of mammals, particularly. of man, in concentrations ranging from 15 to 40 mmoles/kg of tissue. Chemically, carnosine consists of a dipeptide, namely β-alanylhistidine." (Setra at page 2, lines 3 – 10.)

Setra teaches that the purpose of β-alanylhistidine helps prevent muscle fatigue by to buffering proton release during the generation of ATP from ADP and the generation of lactic acid during anaerobic activity (page 2, lines 7 – 13).

Setra does not expressly disclose the administration of β-alanine in the compositions that already include L-histidine and carnosine (Examples 1, 2 and 4) even though Setra does disclose the inclusion of essential or non-essential amino acids (page 2, lines 28 – 34)

However, Asatoor in the same field of endeavor discloses dietary compositions (a mixture) comprising β-alanine and L-histidine (free amino acids) (Abstract and Methods). Asatoor further discloses that the absorption of the free amino acids (β-alanine and L-histidine) is significantly more rapid that the dipeptide (carnosine) (pages 250 and 252).

It would have been obvious to the person of ordinary skill in the art at the time of the invention to modify the compositions of Setra by including free β–alanine and L-histidine as taught by Asatoor in order to promote the synthesis of carnosine in muscle tissue thereby reducing the onset of muscle fatigue. Thus, **claim 12** is *prima facie* obvious over Setra in view of Asatoor, absent evidence to the contrary.

Claim 13 depends from claim 12 and further requires that the method comprise providing to a subject a composition containing L-histidine. Both Setra (Examples 1, 2 and 4) and Asatoor (pages 250 and 252) disclose providing L-histidine to a subject. Setra discloses that it is well known that β–alanine and L-histidine will combine to form

carnosine (β-alanylhistidine). Thus, the ingestion of β-alanine and histidine will necessarily promote the synthesis of carnosine in muscle tissue.

Claim 14 depends from claim 12 and further requires increasing the concentration of creatine in the muscle tissue. The compositions of Examples 1 and 2 in Setra include creatine, which, when ingested, will necessarily lead to an increase in creatine in muscle tissue.

Claim 15 depends from claim 14 and further requires providing an amount of L-histidine to the blood or blood plasma effective to increase β-alanylhistidine dipeptide synthesis in muscle tissue. The compositions of Examples 1 and 2 of Setra include both L-histidine and creatine. Thus, Setra in combination with Asatoor teaches the ingestion of creatine, L-histidine as well as β-alanine. The ingestion of L-histidine with creatine and β-alanine will necessarily increase β-alanyl-histidine dipeptide synthesis in muscle tissue.

Claim 16 depends from claim 12 and further requires "increasing the amount of creatine to the muscle tissue includes providing an amount of creatine to the blood or blood plasma effective to increase the concentration of creatine in the muscle tissue." The compositions of Examples 1 and 2 of Setra contain creatine. The ingestion of a composition containing creatine will necessarily increase the concentration of creatine in the blood or blood plasma and then increase the amount of creatine in the muscle tissue.

Claim 17 depends from claim 12 and further requires that the method step involve the oral administration of the composition. Setra teaches that the composition Example 1 can be orally administered to the subject (page 2, lines 49 – 58).

Claim 18 depends from claim 12 and further requires that the providing step is by infusion. The administration by infusion of sterile compositions designed to reduce muscle fatigue is also an obvious alternative to oral administration.

Claim 19 depends from claim 12 and further requires that the subject is a human. Setra discloses compositions that are pharmaceutical, dietetic and veterinary compositions which suggests administration to humans or animals (page 2).

In summary, claims 12 – 19 of the '422 patent are **prima facie** obvious over Setra in view of Asatoor.

Issue No. 8: Adopted

The Third Party Requester proposes that claims 12 – 19 are obvious over Setra in view of Gardner as set forth in the request at pages 29 and 31 – 33. Issue No. 8 **is adopted** for the following reasons.

Claims 12 – 19 are rejected under 35 USC 103(a) as being unpatentable over Setra in view of Gardner.

Setra discloses pharmaceutical, dietetic or veterinary compositions containing carnosine or peptides related thereto as the active ingredient (page 2, lines 1 - 2). The compositions of Examples 1 and 2 comprise both carnosine and L-histidine (page 2, lines 25 - 37). In particular, Setra discusses the known beneficial properties of these compositions when they are ingested: "Carnosine is a physiological substance, which is

present in muscles and in some nervous tissues of mammals, particularly. of man, in concentrations ranging from 15 to 40 mmoles/kg of tissue. Chemically, carnosine consists of a dipeptide, namely β-alanylhistidine." (Setra at page 2, lines 3 – 10.) Setra teaches that the purpose of β-alanylhistidine helps prevent muscle fatigue by to buffering proton release during the generation of ATP from ADP and the generation of lactic acid during anaerobic activity (page 2, lines 7 – 13).

Setra does not expressly disclose the administration of β-alanine in the compositions that already include L-histidine and carnosine (Examples 1, 2 and 4) even though Setra does disclose the inclusion generally of essential or non-essential amino acids (page 2, lines 28 – 34)

Gardner discloses a human subject ingesting a dietary supplement comprising beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide, as required by claim 12 (pages 412 - 413).

It would have been obvious to the person of ordinary skill in the art to modify the compositions of Setra by including free β-alanine as taught by Gardner in order to arrive at a method for delaying the onset of muscular fatigue in a subject by providing a dietary supplement comprising β-alanine and L-histidine that will necessarily, when ingested, increase blood concentration of β-alanine and L-histidine and subsequently increase the synthesis of β-alanylhistidine in muscle tissue, thereby delaying the onset of muscle fatigue. Thus, claim 12 is prima facie obvious over Setra in view of Gardner.

Claim 13 depends from claim 12 and further requires "providing an amount of L-histidine to the blood or blood plasma effective to increase β-alanylhistidine synthesis in muscle tissue."

Examples 1 and 2 of Setra describe compositions containing L-histidine. When the composition of Examples 1 or 2 of Setra is combined with the free β-alanine taught by Gardner, there is an improved composition that will necessarily provide an amount of L-histidine to the blood or blood plasma effective to increase β-alanylhistidine synthesis in muscle tissue.

Claim 14 depends from claim 12 and further requires that the composition of the method increase the concentration of creatine in the muscle tissue.

Examples 1 and 2 of Setra contain creatine. When the free β-alanine described in Gardner is combined with either Example 1 and 2 of Setra, a composition is created that, will ingested, will necessarily increase the concentration of creatine in the blood or blood plasma effective to increase β-alanylhistidine synthesis in muscle tissue.

Clam 15 depends from claim 14 and further requires that the method of claim 12 provides an amount of L-histidine to the blood or blood plasma effective to increase β-alanylhistidine dipeptide synthesis in the muscle tissue.

Examples 1 and 2 of Setra comprise L-histidine. When the free β-alanine described in Gardner is combined with either Example 1 and 2 of Setra, a composition is created that, when ingested, will necessarily increase the concentration of L-histidine in the blood or blood plasma effective to increase β-alanylhistidine synthesis in muscle tissue.

Claim 16 depends from claim 12 and further requires that increasing the amount of creatine in the muscle tissue includes providing an amount of creatine to the blood or blood plasma effective to increase the concentration of creatine in the muscle tissue.

Examples 1 and 2 of Setra contain creatine. When the free β-alanine described in Gardner is combined with either Example 1 and 2 of Setra, a composition is created that, will ingested, necessarily increase the concentration of creatine in the blood or blood plasma and then increase the concentration of creatine in muscle tissue effective to increase β-alanylhistidine synthesis in muscle tissue.

Claim 17 depends from claim 12 and further requires that the administration is by ingestion.

Setra discloses that the administration of the dietary composition is by ingestion (page 2, line 29).

Claim 18 depends from claim 12 and further requires that the administration is by infusion.

The administration by infusion of sterile compositions designed to reduce muscle fatigue is also an obvious alternative to oral administration (page 2, lines 29).

Claim 19 depends from claim 12 and further requires that the subject is a human.

Setra discloses compositions that are pharmaceutical, dietetic and veterinary compositions which suggests administration to humans or animals (page 2).

In summary, claims 12 – 19 of the '422 patent are *prima facie* obvious over Setra in view of Gardner.

Issue No. 9: Adopted

The Third Party Requester proposes that claim 12 of the '422 patent is obvious over Setra in view of Asatoor and Gardner as set forth in the request at pages 28 - 33. Issue No. 9 **is adopted** for the following reasons.

As explained under Ground of Rejection Nos. 7 and 8, claim 12 is obvious over Setra in view of Asatoor as well as Setra in view of Gardner. Therefore, logic requires that claims 12 is also obvious over Setra in view of Asatoor and Gardner.

Ground of Rejection #10:

The Third Party Requester proposes that claims 12 – 19 of the '422 patent are obvious over Setra in view of Bauer or Bakardjiev as set forth in the request at pages 29 – 33. Ground of Rejection No. 9 **is adopted** for the following reasons.

Claims 12 – 19 are rejected under 35 USC 103(a) as being unpatentable over Setra in view of Bauer or Bakarjiev.

Setra discloses pharmaceutical, dietetic or veterinary compositions containing carnosine or peptides related thereto as the active ingredient (page 2, lines 1 - 2). The compositions of Examples 1 and 2 comprise both carnosine and L-histidine (page 2, lines 25 - 37). In particular, Setra discusses the known beneficial properties of these compositions when they are ingested: "Carnosine is a physiological substance, which is present in muscles and in some nervous tissues of mammals, particularly, of man, in concentrations ranging from 15 to 40 mmoles/kg of tissue. Chemically, carnosine consists of a dipeptide, namely β-alanylhistidine." (Setra at page 2, lines 3 – 10.)

Setra teaches that the purpose of β-alanylhistidine helps prevent muscle fatigue by to buffering proton release during the generation of ATP from ADP and the generation of lactic acid during anaerobic activity (page 2, lines 7 – 13).

Setra does not expressly disclose the administration of β-alanine in the compositions that already include L-histidine and carnosine (Examples 1, 2 and 4) even though Setra does disclose the inclusion generally of essential or non-essential amino acids (page 2, lines 28 – 34).

Bauer discloses that carnosine is synthesized in tissue from its constituent amino acids, β-alanine and L-histidine, in skeletal muscle cells in primary culture (Abstract).

Bakardjiev also discloses that carnosine is synthesized from its constituent amino acids, β-alanine and L-histidine, in skeletal muscle cells in primary culture (Abstract).

It would have been obvious to the person of ordinary skill in the art to modify the compositions of Setra by including free β-alanine as suggested by Bauer and Bakarjiev in order to arrive at a method for delaying the onset of muscular fatigue in a subject by providing a dietary supplement comprising β-alanine and L-histidine that will necessarily, when ingested, increase blood concentration of β-alanine and L-histidine and subsequently increase the synthesis of β-alanylhistidine in muscle tissue, thereby delaying the onset of muscle fatigue. Thus, claim 12 is *prima facie* obvious over Setra in view of Bauer or Bakarjiev.

Claim 13 depends from claim 12 and further requires that the dietary composition provide an amount of L-histidine to the blood or blood plasma effective to increase β-alanylhistidine dipeptide synthesis in the muscle tissue.

Setra discloses compositions comprising L-histidine in Examples 1 and 2 on pages 2 and 3. The administration of a composition comprising both L-histidine and β-alanine as suggested by Setra in combination with Bauer or Bakarjiev will necessarily provide an increased amount of L-histidine to the blood or blood plasma resulting in increased β–alanylhistidine dipeptide synthesis in muscle tissue.

Claim 14 depends from claim 12 and further requires that said method comprises increasing the concentration of creatine in the muscle tissue.

Examples 1 and 2 of Setra contain both L-histidine and creatine. The administration of a composition of Example 1 or 2 of Setra in combination with free β-alanine as taught by Bauer or Bakarjiev will necessarily lead to an increase in creatine in muscle tissue.

Claim 15 depends from claim 14 and further requires "providing an amount of L-histidine to the blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in the muscle tissue."

Examples 1 and 2 of Setra contain both L-histidine and creatine. The administration of a composition of Example 1 or 2 of Setra in combination with free β-alanine as taught by Bauer or Bakarjiev will necessarily lead to an increase in L-histidine in blood or blood plasma effective to increase β-alanylhistidine dipeptide synthesis in muscle tissue.

Claim 16 depends from claim 12 and further requires that said method comprises "increasing the amount of creatine in the muscle tissue includes providing an

amount of creatine to the blood or blood stream effective to increase the concentration of creatine in the muscle tissue."

Examples 1 and 2 of Setra contain both L-histidine and creatine. The administration of a composition of Example 1 or 2 of Setra in combination with free β-alanine as taught by Bauer or Bakarjiev will necessarily lead to an increase in creatine in muscle tissue, which includes providing an amount of creatine to the blood or blood plasma effective to increase the concentration of creatine in muscle tissue.

Claim 17 depends from claim 12 and further requires that the providing step is by ingestion.

Setra discloses that the administration of the dietary composition is by ingestion (page 2, line 29).

Claim 18 depends from claim 12 and further requires that the providing step is by infusion.

Although Setra discloses oral administration of the pharmaceutical compositions, such compositions could obviously be made into sterile solutions and be administered by IV infusion when an individual cannot ingest the supplement.

Claim 19 depends from claim 12 and further requires that the subject is human.

Setra discloses compositions that are pharmaceutical, dietetic and veterinary compositions which suggests administration to either humans or animals.

In summary, claims 12 – 19 of the '422 patent are *prima facie* obvious over Setra in view of Bauer or Bakardjiev.

Claims Not Under Reexamination

Since requester did not request reexamination of claims 1 - 11 and 20 – 21, such claims are not being reexamined.

Conclusion

Issue Nos. 1 – 5 and 7 - 10 are adopted.

Claims 12 – 19 are rejected. Claims 1 – 11 and 20 – 21 are not under reexamination.

Extensions of Time

Extensions of time under 37 CFR 1.136(a) will not be permitted in *Inter Partes* Reexamination because the provisions of 37 CFR 1.136 apply only to "an applicant" and not to the Patent Owner in a reexamination proceeding. Extensions of time in an *Inter Partes* Reexamination proceeding are otherwise governed by 37 CFR 1.956 for Patent Owner. It should be noted that **extensions of time under 37 CFR 1.956 are not available to the Third Party requester**. Extensions of time are not available for Third Party Requester comments because a comment period of 30 days from service of Patent Owner's response is set by statute (See 35 U.S.C. 314(b)(3)). Additionally, 35 U.S.C. 314(c) requires that Inter Partes reexamination proceedings "will be conducted with special dispatch" (37 CFR 1.937).

Ongoing Duty to Disclose

The Patent Owner is reminded of the continuing responsibility under 37 C.F.R. 1.985(a) to apprise the Office of any litigation activity, or other prior art concurrent proceeding, involving Patent No. 8,129,422 throughout the course of this reexamination proceeding. The Third Party Requester is also reminded of the ability to similarly apprise the Office of any such activity or proceeding throughout the course of this reexamination proceeding. See MPEP §§2686 and 2686.04.

Service on the Other Party (3rd Party Request)

After the filing of a request for reexamination by a third party requester, any document filed by the patent owner or the third party must be served on the other party (or parties) where two or more third party requester proceedings are merged) in the reexamination proceeding in the manner provided in 37 CFR 1.248 (See 37 CFR 1.903 and MPEP 2666.06).

Correspondence

All correspondence relating to this Inter Partes Reexamination proceeding should be directed to:

By Electronic Filing System (EFS):

Registered users may submit via the electronic filing system EPS-Web at https://efs.uspto.gov/efile/myportal/efs-registered

By Mail to:

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Commissioner of Patents
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EFS-Web offers the benefit of quick submission to the particular area of the Office that needs to act on the correspondence. Also, EFS-Web submissions are "soft scanned" (i.e., electronically uploaded) directly into the official file for the reexamination proceeding, which offers parties the opportunity to review the content of their submissions after the "soft scanning" process is complete.

Any inquiry concerning this communication or earlier communication from the examiner, or as to the same of this proceeding, should be directed to the Central Reexamination Unit at telephone number (571) 272-7705.

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